REMARKS/ARGUMENTS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated March 19, 2003 are respectfully requested. Claims 11-14 and 18 are pending and under examination.

I. Amendments

Claim 18 has been amended as set forth above to correct antecedent basis.

No new matter has been added by this amendment.

II. Rejections under 35 U.S.C. § 112, second paragraph

Claims 11-14, 18 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. This rejection is traversed in view of the following.

Claims 11, 12 and 13 were rejected as being unclear in reciting "encoding a polypeptide derived from the carboxy-terminal 549 amino acids of HEV reading frame 2" for not disclosing what modifications may fall within the limitation intended by "derived."

It is a fundamental principle under Section 112, second paragraph, that inventors may act as their own lexicographers. *Lear Siegler, Inc. v. Aeroquip Corp.*, 733 F.2d 881, 221 USPQ 1025, 1031 (Fed. Cir. 1984); *Fromson v. Advance Offset Plate, Inc.*, 7210 F.2d 1565, 1549, 219 USPQ 1137, 1140 (Fed. Cir. 1983). Inventors may generally define claim terminology in whatever terms they consider suitable. Furthermore, in determining the meaning of patent claims, words or phrases in a claim will be given their ordinary meaning unless the specification indicates that the inventor used these words or phrases differently. *Jonsson v. Stanley Works,* 903 F.2d 812, 14

USPQ 2d 1863, 1871 (Fed. Cir. 1990) (citing *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 759, 221 USPQ 473, 477 (Fed. Cir. 1984)).

Section I, entitled "Definitions," of the detailed description of the invention defines the term "derived from" as follows:

> A polynucleotide is "derived from" HEV if it has the same or substantially the same basepair sequence as a region of an HEV genome, cDNA of HEV or complements thereof, or if it displays homology as noted under "B" or "C" above. (page 16, lines 17-21)

Sections B and C, on page 14, line 1 – page 15, line 23 explain the meaning of homology as follows:

> "Sequence homology" is determined essentially as follows. Two polynucleotide sequences of the same length (preferably, the entire viral genome) are considered to be homologous to one another, if, when they are aligned using the ALIGN program, over 40%, preferably 50%, or more preferably 70% of the nucleic acids in the highest scoring alignment are identically aligned using a ktup of 1, the default parameters and the default PAM matrix.
>
> The ALIGN program is found in the FASTA version 1.7 suite of sequence comparison programs (Pearson, et al., 1988; Pearson, 1990; program available from William R. Pearson, Department of Biological Chemistry, Box 440, Jordan Hall, Charlottesville, Va.).
>
> In determining whether two viruses are "highly homologous" to each other, the complete sequence of all the viral proteins for one virus are optimally, globally aligned with the viral proteins or polyprotein of the other virus using the ALIGN program of the above suite using a ktup of 1, the default parameters and the default PAM matrix. Regions of dissimilarity or similarity are not excluded from the analysis. Differences in lengths

between the two sequences are considered as mismatches. Alternatively, viral structural protein regions are typically used to determine relatedness between viral isolates. Highly homologous viruses have over 40%, or preferably 50%, or more preferably 70% global polypeptide sequence identity.

Two nucleic acid fragments are considered to be "selectively hybridizable" to an HEV polynucleotide, if they are capable of (1) specifically hybridizing to HEV or a variant thereof or (2) specifically priming a polymerase chain reaction: (i) under typical hybridization and wash conditions, as described, for example, in Maniatis, et al., pages 320-328, and 382- 389, (ii) using reduced stringency wash conditions that allow at most about 25- 30% basepair mismatches, for example: 2*SSC, 0.1% SDS, room temperature twice, 30 minutes each; then 2*SSC, 0.1% SDS, 37[deg] C. once, 30 minutes; then 2*SSC room temperature twice, 10 minutes each, or (iii) selecting primers for use in typical polymerase chain reactions (PCR) under standard conditions (for example, in Saiki, R. K, et al.; Mullis, et al.), which result in specific amplification of sequences of HEV or its variants.

The degrees of homology (sequence identity) discussed above can be selected for by hybridization using wash conditions of appropriate stringency for identification of clones from gene libraries (or other sources of genetic material), as is well known in the art.

Thus, in the instant case, Applicants have properly defined the claim term "derived from" as noted above such that it is sufficiently clear.

Claim 18 has been rejected as indefinite for lacking antecedent basis. The claim has been amended to recite the expression vector of claim 12, thereby obviating the rejection.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

II. Rejection Under 35 U.S.C. §112, first paragraph

Claims 11-14 and 18 were rejected under 35 U.S.C. §112, first paragraph as being enabling for a substantially isolated nucleic acid molecule encoding a polypeptide consisting of the carboxy terminal 549 amino acids of HEV open reading frame 2, but as not providing enablement for a substantially isolated nucleic acid molecule encoding a polypeptide derived from the carboxy terminal 549 amino acids of HEV open reading frame 2. The Examiner asserts that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims; and that "derived" is characterized as indefinite and given the broadest interpretation.

This rejection is traversed in view of the following.

The test of enablement is whether the disclosure is sufficient to teach one skilled in the art how to make and/or use the invention as claimed.

"How to make" requirement

It is clear from the sequences provided in the Sequence Listing and from the explanation of the meaning of "derived from" (*e.g.*, page 16, lines 17-21, and page 14, line 1 – page 15, line 17 of the instant specification, as described in detail above), what nucleic acid sequences are covered by the claim. One skilled in the art could readily produce any of these nucleic acid sequences using a variety of well-known methods, including the recombinant methods disclosed throughout the specification, and test them for the required homology as disclosed in, for instance, page 14, line 1 – page 15, line 23 of the specification.

Applicants thus submit that the specification complies with the "how to make" requirement of 35 U.S.C. §112, first paragraph.

"How to use" requirement

The "how to use" requirement is met unless an undue number of claimed species are inoperative. In this case, inoperative species are defined as those that fail to meet the homology requirements as set forth on page 14, line 1 – page 15, line 23 of the specification.

As a matter of Patent Office practice... a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971).

The Examiner has provided no reasonable basis for casting doubt on the operability of the claimed species. Accordingly, since both the "how-to-make" and "how-to-use" requirements are met, Applicants submit that the specification meets the enablement requirements of 35 U.S.C. §112, first paragraph.

III. Rejections under 35 U.S.C. § 102(e)

Claims 11-14 and 18 were rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,514,690 to Li *et al.* This rejection is respectfully traversed in light of the following remarks.

35 U.S.C. §102(e) states that a person is entitled to a patent unless the invention was described in a patent granted on an application for patent by another filed on an international application by another who has fulfilled the requirements of paragraphs 1, 2 and 4 of section 371(c) *before* the invention thereof by the applicant for patent.

Claims 11-14 and 18 are directed to isolated nucleic acid sequences, expression vectors, expression systems and methods of producing HEV which include sequences "derived from" the carboxy terminus of the second reading frame of ORF2. As discussed above, the term "derived from" includes a number of sequences that were

identified in the related applications having a priority date prior to September 23, 1994, e.g., U.S. application number 08/240,049, filed May 9, 1994, which issued as U.S. Patent No. 5,686,239 ('239). The '239 application specifically identifies the C-terminal region of the second ORF, and discloses the full-length nucleotide ORF2 sequence which includes the 549 C-terminus, as well as a number of other C-terminal fragments. Thus, the claims of the instant invention should be given a priority date, at the latest, of May 9, 1994. This date is earlier than Li, *et al.*, which has a filing date of September 23, 1994.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102.

In view of the foregoing, the claims pending in the application comply with the requirements of 35 U.S.C. § 112 and patentably define over the cited art. A Notice of Allowance is, therefore, respectfully requested. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 838-4405.

Respectfully submitted,
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Date: 6-18-03

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

18. (Amended) A method of producing a Hepatitis E Virus (HEV) polypeptide composition, comprising the steps of:

culturing a cell containing the expression vector of claim ~~11~~ 12 under conditions sufficient to express a polypeptide sequence encoded by said nucleic acid.